SEXUALLY TRANSMITTED INFECTIONS

Authors: Victoria Wesevich MD, and Christina Ackerman, MD

Introductory Case

A 20-year-old G0 presents for her first gynecology visit to establish well-woman care. She is sexually active with both male and female partners and is not currently using any contraception. She is asymptomatic and does not currently desire pregnancy.

How do you counsel her about risks of unprotected sexual activity and indicated screening tests for sexually transmitted infections (STIs)?

Milestone-Based Focused Questions

LEVEL 1: DEMONSTRATES BASIC KNOWLEDGE ABOUT COMMON AMBULATORY OB/GYN CONDITIONS

WHAT ARE THE COMMON STIS?

There are many sexually transmitted infections (STIs). The most common STIs include human papilloma virus (HPV), syphilis, trichomonas vaginalis, chlamydia trachomatis (CT), neisseria gonorrhea (GC), hepatitis B, hepatitis C, human immunodeficiency disease (HIV), and herpes simplex virus (HSV).

WHAT IS THE INCIDENCE OF THESE STIS?

STIs continue to increase in frequency in the United States and represent a major public health concern for young women. Based on the Centers for Disease Control and Prevention (CDC) surveillance statistics, more than 2 million cases of STIs were reported in 2016 in the United States. This is the highest incidence of STIs to date and represents a preventable threat to young women's reproductive health and fertility.

Specifically, since 2013, there has been a 22% increase in cases of chlamydia, a 67% percent increase in cases of gonorrhea, and a 76% increase in cases of syphilis. Not only has the incidence of STIs increased but the ability to successfully treat these infections has decreased as antibiotic resistance spreads.

Incidence of Sexually Transmitted Infections in the United States

STI	Incidence in 2018 (n)	Cases per 100,000 people
Chlamydia	1,758,668	540
Gonorrhea	583,405	179
Syphilis (all stages)	115,0451	35
Congenital	1,306	33
Trichomonas	1,090,000	11
HIV	38,500	0.38
Hepatitis B	21,600	1
Hepatitis C	50,300	1.2

WHAT ARE THE PRESENTING SYMPTOMS OF THESE STIS?

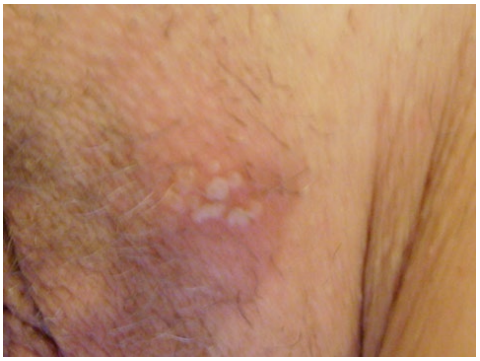
The breadth and depth of STIs are varied, and the symptoms may be different for men and women. Additionally, there are patients who may be asymptomatic carriers.
For STIs that cause cervicitis (GC, CT, trichomonas), women may experience malodorous or discolored vaginal discharge, vaginal pruritis or burning, or dysuria. They may also present with generalized pelvic pain.
Acute infection with HIV is characterized by fever, lymphadenopathy, sore throat, rash, myalgia/arthralgia, diarrhea, and headache. However, a significant proportion of patients with early HIV infection will be asymptomatic.
The initial clinical manifestation of syphilis infection is a localized skin lesion known as a ***chancre***. The median incubation period before the chancre appears is 21 days with a range of 3 to 90 days. The lesion begins at the site of inoculation as a papule, which is typically painless, and soon ulcerates to produce the classic chancre of primary syphilis. The chancre is a 1 to 2-centimeter ulcer with a raised, indurated margin, which generally has a non-exudative base. The patient may also have mild to moderate regional lymphadenopathy that is often bilateral.


Syphilis chancre (image licensed for public use through Creative Commons)

The typical clinical symptoms of acute hepatitis B and C include malaise, fatigue, anorexia, nausea, right upper quadrant or epigastric pain, jaundice, hepatomegaly, dark urine and/or gray/acholic stool.

For HPV, many women are asymptomatic and are diagnosed only through routine cervical cancer screening. Alternatively, patients may present with visible genital condyloma (warts).

The primary genital HSV infection often presents with multiple painful genital vesicles that progress to ulcers, in addition to other symptoms of fever, local lymphadenopathy, painful urination, and headache. Subsequent outbreaks are typically milder and may be asymptomatic.


Vesicles of initial HSV outbreak (image licensed for public use through Creative Commons)

Modes of transmission may vary among the types of STIs. HSV can be transmitted through direct contact with mucous membranes, even without sexual intercourse. In addition, viral shedding can occur even without active

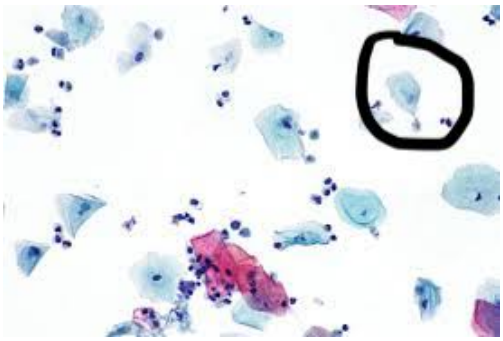
lesions or even prodromal symptoms. Similarly, HPV can be transmitted through direct contact, in the absence of vaginal intercourse.

HOW CAN PATIENTS PREVENT STIS?

Patient education is a crucial component to any gynecologic care. The correct use of barrier protection, including condoms and dental dams, are critical to preventing the spread of STIs. It is important that patients understand that other forms of contraception including oral hormonal contraception, intrauterine devices, injectables and implants do not prevent the spread of STIs. In addition, condoms are less effective in protecting against STIs that are spread via skin-to-skin contact such as such as HSV and external HPV.

HOW DO YOU TEST FOR GONORRHEA, CHLAMYDIA AND TRICHOMONAS?

Diagnosis of GC, CT, or trichomonas is made based on nucleic acid amplification test (NAAT) on either first catch (dirty) urine specimen or vaginal/cervical swabs (collected by a medical provider or obtained via self-swab). In addition, trichomonas can be diagnosed with wet-mount microscopy; however, NAAT testing is more sensitive.



Wet mount demonstrating trichomonads (image licensed for public use through Creative Commons)

HOW DO YOU TEST FOR HIV, HEPATITIS B, AND HEPATITIS C?

HIV is diagnosed using the **HIV-1/2 antigen/antibody immunoassay**. Confirmatory testing is performed using RNA virus detection.

For hepatitis B, the initial screening test is a serum test for Hepatitis B Surface Antigen (**HBsAg**). HBsAg is detectable up to four weeks prior to clinical symptoms and remains detectable for 1-6wks. Chronic hepatitis B is defined by persistence of HBsAg and absence of Hepatitis B Surface IgG Antibody (Anti-HBs). When determining whether the patient will develop a chronic carrier state after acute infection, presence of HBsAg for >20 weeks is predictive of the chronic carrier state. Of note, during clearance of resolving infection a 'window period' can occur during which HBsAg and Anti-HBs are undetectable. During this time, infection can be identified by detection of Hepatitis B Core IgG (Anti-HBc), which develops much more quickly than Anti-HBs.

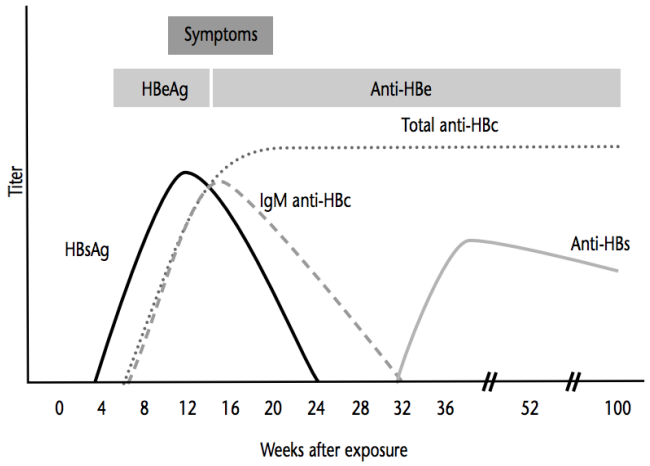


Figure 1. Typical serologic course of acute hepatitis B virus infection with recovery. (Centers for Disease Control and Prevention slide set adapted from Mast EE, Weinbaum CM, Fiore AE, Alter MJ, Bell BP, Finelli L, et al. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices [ACIP] part II: immunization of adults. MMWR Recomm Rep 2006;55(RR-16):1–33; quiz CE1–4.)

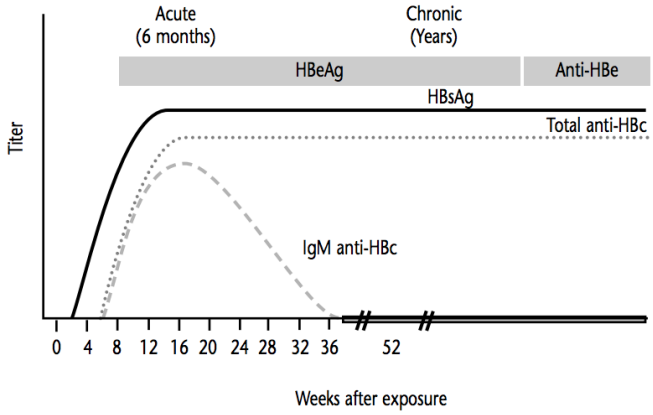


Figure 2. Progression to chronic hepatitis B virus infection: typical serologic course. (Centers for Disease Control and Prevention slide set adapted from Mast EE, Weinbaum CM, Fiore AE, Alter MJ, Bell BP, Finelli L, et al. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) part II: immunization of adults. MMWR Recomm Rep 2006;55(RR-16):1–33; quiz CE1-4.

(Source: ACOG Practice Bulletin 86 Viral Hepatitis in Pregnancy)

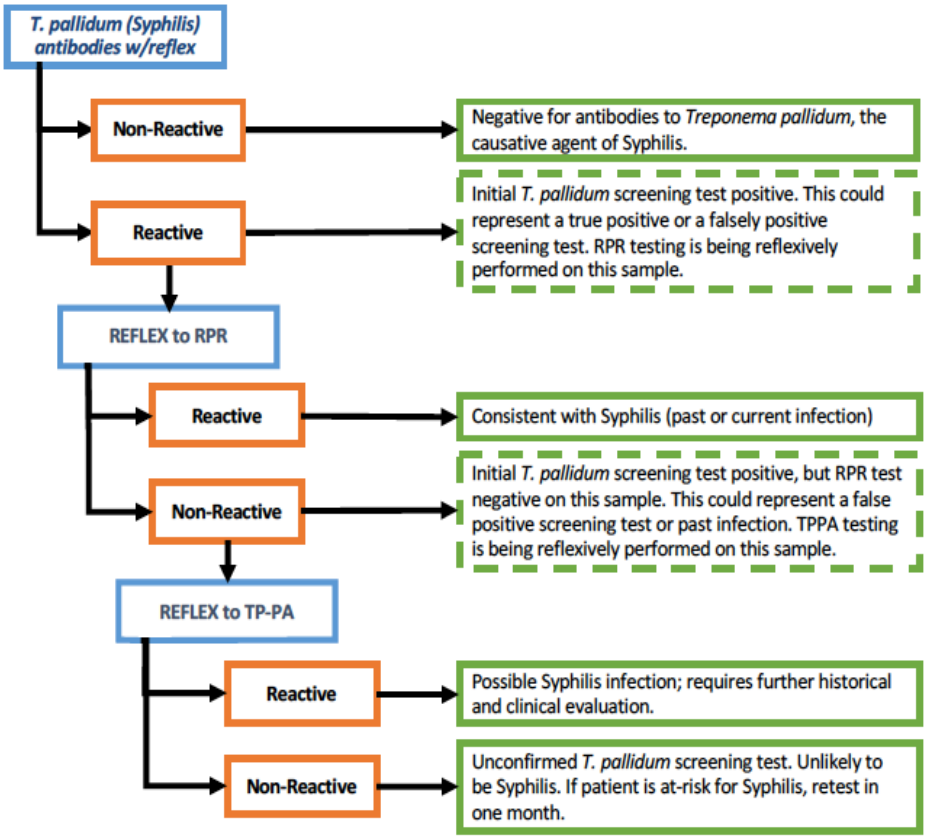
The initial screening test for hepatitis C virus (HCV) is a serum test for Hepatitis C Antibody (HepC Ab). A reactive or indeterminate/equivocal antibody test should be followed by HCV RNA testing. Patients suspected of having acute hepatitis C are more likely to have a false-negative antibody testing, as do severely immunocompromised patients and patients undergoing hemodialysis. It is recommended that these patients have HCV RNA testing sent concurrently with antibody testing. If HCV RNA is detected, the diagnosis of HCV infection is confirmed. If HCV RNA is not detected in a patient with a positive Hep C Ab, then a reactive antibody likely represents either a prior HCV infection that subsequently cleared or a false-positive.

HOW DO YOU TEST FOR SYPHILLIS?

Traditionally, syphilis test algorithms have started with a non-treponemal assay (e.g. VDRL or RPR) that detects antibodies to lipoidal antigens. Positive tests were reflexed to a treponemal assay (e.g FTA-ABS, or TP-PA) that detects Treponema pallidum-specific antigens. However, non-treponemal tests have inherent limitations: they lack sensitivity in primary and late syphilis, are not specific to syphilis, and are manual, labor-intensive tests. Thus, many labs use a "reverse" syphilis test algorithm. This involves initial screening with treponemal antibody screen, often a chemiluminescence immunoassay that looks for total antibodies (both IgG and IgM) to T. pallidum. "Reactive" specimens will be reflexively tested by RPR, a non-treponemal test, to

assess disease activity. Discordant samples (Antibody+/ RPR-) will be tested using a second T. pallidum assay, TP-PA, to confirm screen specificity.

From the Office of Clinical Microbiology, Yale New Haven Hospital, 2016 (permission obtained)



LEVEL 2: DEMONSTRATES KNOWLEDGE OF APPROPRIATE SCREENING GUIDELINES.

WHAT ARE THE CURRENT RECOMMENDATIONS FOR STI SCREENING?

You discuss screening options with the patient and decide to test for GC, CT, and trichomonas.
The patient's test for GC returns positive. All other tests are negative.

CDC Screening Recommendations for STIs

HIV	*All women age 13-64 should be screened at least once*	*Annual screening for patients who engage in unsafe sex*	*Annual screening for patients who share equipment for IV drug use*	*Twice in pregnancy (initial OB visit and 3rd trimester)*
GC/CT	Annual Screening All women < 25 yo	Annual Screening All women > 25 yo with risk factors	Twice in pregnancy (Initial OB visit and 3rd trimester) for all women <25 yo or >25yo with risk factors	

Trichomonas	Consider for women in high prevalence setting	Consider for women who engage in unsafe sex		
Syphilis	Annual screening for any patient with HIV	Pregnancy (at least once and also in the 3rd trimester in high prevalence areas)		
Hepatitis B	All pregnant women at initial OB visit	Annual screening for patients who engage in unsafe sex	Annual screening for patients who share equipment for IV drug use	At least once in patients with risk factors (no history of vaccination, elevated liver enzymes of unclear etiology, born in high prevalence region, immunocompromised patients)
Hepatitis C	All patients born between 1945 and 1965	Annual screening for patients who share equipment for IV drug use	At least once in patients with risk factors (history of blood transfusion prior to 1992, long-standing hemodialysis, mother with Hep C, receipt of unregulated tattoo)	
HPV	Refer to ASCCP guidelines for cervical cancer screening			

HOW DO YOU COUNSEL YOUR PATIENT ON ADDITIONAL SCREENING TESTS?

It is recommended that any patient with a positive STI screen be offered the full spectrum of STI testing.

LEVEL 3: INTERPRETS APPROPRIATE SCREENING TESTS.

HOW DO YOU COUNSEL YOUR PATIENT ON A POSITIVE GONORRHEA TEST?

Counseling should include the following:

- Gonorrhea is a sexually transmitted infection
- Gonorrhea is curable with appropriate treatment
- Partners should be notified, and expedited partner therapy should be discussed and offered
- Reinfection is possible if the partner(s) are not tested or treated
- There is risk of continued transmission if untreated
- Condom use is recommended in the future to avoid reinfection or acquiring other STIs
- The CDC recommends retesting in 3 months

WHAT ARE THE RECOMMENDATIONS FOR TREATMENT FOR GONORRHEA?

Since antibacterial resistance to treatment for GC has been rising, the American College of Obstetricians and Gynecologists (ACOG) and CDC recommend dual therapy for gonorrhea infection with ceftriaxone and azithromycin. In addition, they recommend both medications be administered on the same day and under direct observation.

CDC Treatment Recommendations

	Standard Rx	Alternative Rx	In Pregnancy
Gonorrhea	Ceftriaxone 500 mg IM (one dose) and Doxycycline 100 mg PO twice daily for 7 days if chlamydia has not been excluded.	Cefixime 400mg PO (one dose) and Azithromycin 1g PO (one dose) or Gentamycin 240mg IM (one dose) and Azithromycin 1g PO (one dose)	Ceftriaxone 250mg IM (one dose) and Azithromycin 1g PO (one dose)
Chlamydia	Azithromycin 1g PO (one dose)	Doxycycline 100mg PO (twice daily for 7 days) or Erythromycin base 500mg PO (4 times daily for 7 days)	Azithromycin 1g PO (one dose) or Amoxicillin 500mg PO (3 times daily for 7 days)
Trichomonas	Metronidazole 2g PO (one dose) or Tinidazole 2g PO (one dose)	Metronidazole 500mg PO (twice daily for 7 days)	Same as non-pregnant
Syphilis Primary, secondary, early latent	Benzathine penicillin 2.4 mil U IM (one dose)	Doxycycline 100mg (twice daily for 14 days for primary and	Penicillin (same as non-pregnant) - if allergy, patient

Late latent, latent of unknown duration, or tertiary	Benzathine penicillin 2.4 mil U IM (weekly for three weeks)	secondary, 28 days for early and late latent) For tertiary, consult infectious disease	should have desensitization For primary, secondary, and early latent, an initial dose one week after the initial dose should be considered in pregnancy
HSV **First Episode** **Recurrent Episode**	Acyclovir 400mg PO (tid for 7-10 days) or Acyclovir 200mg PO (five times a day for 7-10 days) or Valacyclovir 1g PO (BID for 7-10 days) or Famciclovir 250mg PO (TID for 7-10 days) Treatment may be extended if healing is incomplete Acyclovir 400mg PO (3 times daily for 5 days) or Acyclovir 800mg PO (twice daily for 5 days) or Acyclovir 800mg PO (3 times daily for 2 days) or		Same as non-pregnant

Suppressive Therapy	Valacyclovir 500mg PO (twice daily for 3 days) or Valacyclovir 1g PO (daily for 5 days) or Famciclovir 125mg PO (twice daily for 5 days) or Famciclovir 1gm PO (twice daily for 1 day) or Famciclovir 500mg PO once, followed by 250mg twice daily for 2 days Acyclovir 400mg PO (twice daily) or Valacyclovir 500mg - 1gm PO daily (500mg may be less effective) or Famiciclovir 250mg PO (twice daily)		Start at 36 weeks gestation Acyclovir 400mg PO (3 times daily) or Valacyclovir 500mg PO (twice daily) Starting at 36 weeks gestation

HIV	**Refer immediately to HIV clinical-care provider**
	Counsel on post-exposure prophylaxis (PREP) for partner
	Counsel on importance of using condoms and other safe sex practices
Hepatitis	
Hepatitis A	Supportive care: Hydration and cessation of liver toxic medications

Hepatitis B	Acute: Supportive care
	Chronic: Referral to appropriate clinical care provider for possible treatment
Hepatitis C	Referral to appropriate clinical care provider for possible treatment
HPV	Management per ASCCP guidelines

Similarly, it is important to educate patients that they must wait 7 days after treatment for an STI before resuming sexual intercourse. In addition, it is important for the partner to be treated. Otherwise, there is a significant risk of further spread of the infection or reinfection from an untreated partner.

WHAT ARE THE INDICATIONS FOR REPEAT TESTING?

It is crucial for providers to understand the distinction between test-of-cure and retesting to diagnose a repeat infection. Non-pregnant patients with gonorrhea infection who underwent appropriate treatment do not require a test of cure; however, it is recommended that patients undergo repeat testing at 3 months because reinfection rates are very high. Conversely, treatment failure rates are low if patients undergo appropriate dual therapy treatment.

CDC Recommendations for Follow-up

	Gonorrhea	Chlamydia	Trichomonas
Pregnant	3-4 weeks test of cure AND 3 months re-testing	3-4 weeks test of cure AND 3 months re-testing	Test of cure not recommended 3 months re-testing recommended
Not Pregnant	3 months re-testing	3 months re-testing	3 months re-testing

LEVEL 4: CARES FOR PATIENTS WITH COMPLEX PRESENTATIONS, USES A MULTI-DISCIPLINARY APPROACH AND MAKES APPROPRIATE REFERRALS.

HOW DO YOU COUNSEL A PATIENT WITH A POSITIVE GONORRHEA TEST IN PREGNANCY?

Gonorrhea is a treatable and curable disease. It is important for both the pregnant patient and her partner to be treated adequately and for the patient to undergo both a test of cure at 3 weeks and a test of reinfection at 3 months.

Gonorrhea infection during pregnancy can have significant maternal and fetal complications including increased risk for septic abortion, intra-amniotic infection, preterm birth, premature rupture of membranes and postpartum infection. Possible neonatal complications are conjunctivitis, pharyngitis, and gonococcemia.

HOW DO YOU COUNSEL A PATIENT ABOUT OPTIONS FOR PARTNER TREATMENT?

There are many options for testing and treating a patient's sexual partner(s), including referral to regional health department clinics, the partner's primary care provider, or reproductive health clinics such as Planned Parenthood.

Another option is Expedited Partner Treatment (EPT). EPT is the practice of treating sexual partners of patients diagnosed with chlamydia, gonorrhea, or trichomonas infection without first examining or testing the partner. EPT should include patient counseling and written treatment instructions for the patient's partner. The partner should also be encouraged to seek medical evaluation for screening for other STIs, such as HIV, syphilis and hepatitis. Several studies have demonstrated the efficacy of EPT at decreasing reinfection rates as compared to standard partner referrals to another provider.

Unfortunately, there are several practical, administrative, and legal barriers to implementation of EPT; and states have different laws regarding EPT. Physicians should familiarize themselves with their state's laws regarding EPT. Despite recommendations from ACOG and the potential to alleviate a major public health concern by utilizing EPT, implementation of EPT is low.

WHAT ARE THE EXCLUSION CRITERIA FOR USE OF EPT?

- Men who have sex with men (MSM)
- History of a known severe allergic reaction to azithromycin, cephalosporins, or penicillin
- Risk of intimate partner violence associated with partner notification
- Suspected cases of child abuse or sexual assault

IS EPT APPROPRIATE FOR ADOLESCENTS?

Yes. EPT is safe, legal, and efficacious among minors. The Society of Adolescent Health and Medicine and the American Academy of Pediatrics both support the use of EPT in adolescents. In addition, based on several randomized controlled trials, the effectiveness of EPT in adolescents is similar to that of adults. It results in equivalent or slightly improved rates of reinfection for gonorrhea and chlamydia compared with standard partner notification.

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